L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AB A method for recovering a weak organic acid (such as a low-mol.-weight alc.) from a fermentation broth or other aqueous solution containing ≤40% by volume of the organic acid comprises **dissolving a base** or a basic salt of an acid having a pKa >6 in the fermentation broth in an amount of ≥ 26 g/100 mL solution This results in a 2-phase system comprising a lower phase rich in base (or basic salt) and an upper phase rich in the weak organic acid. The organic acid is then recovered from the upper phase. The method is particularly useful for the recovery of EtOH from fermented biomass, for example in an integrated EtOH-water separation/fermentation effluent waste treatment process.

AN 1986:459475 CAPLUS
DN 105:59475

TI Recovery of a weak organic acid from its aqueous solution

IN Reeves, Russell Robert
PA Apace Research Ltd., Australia

SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI EP 173544	A2	19860305	EP 1985-305942		19850821
EP 173544	A3	19860521			
EP 173544	B1	19910522			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
			AU 1984-6711	A	19840822
AU 8545938	A1	19860227	AU 1985-45938		19840822
AU 576377	B2	19880825			
			AU 1984-6711	A	19840822
US 4594466	A	19860610	US 1985-761482		19850801
			AU 1984-6711	A	19840822
IN 165111	A	19890819	IN 1985-MA602		19850802
			AU 1984-6711	A	19840822
BR 8504008	A	19860610	BR 1985-4008		19850821
			AU 1984-6711	A	19840822
CA 1241025	A1	19880823	CA 1985-489142		19850821
			AU 1984-6711	A	19840822
AT 63739	E	19910615	AT 1985-305942		19850821
			AU 1984-6711	A	19840822
			EP 1985-305942	A	19850821

2/17/05

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NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	JAN 26	CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT)
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NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005

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DICTIONARY FILE UPDATES: 15 FEB 2005 HIGHEST RN 831913-30-5

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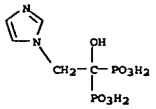
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s zoledronic
L1 2 ZOLEDRONIC

=> d 1-2

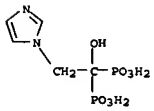
L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 165800-06-6 REGISTRY
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis-, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Zoledronic acid hydrate**
MF C5 H10 N2 O7 P2 . H2 O
SR US Adopted Names Council (USAN)
LC STN Files: BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CIN, EMBASE, IPA, MRCK*, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
CRN (118072-93-8)



● H_2O

1 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 118072-93-8 REGISTRY
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN (1-Hydroxy-2-imidazol-1-ylethylidene)diphosphonic acid
CN 1-Hydroxy-2-(1H-imidazol-1-yl)ethylidene-1,1-bisphosphonic acid
CN CGP 42446
CN Zoledronate
CN **Zoledronic acid**
CN Zometa
FS 3D CONCORD
MF C5 H10 N2 O7 P2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES,
DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Book; Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

334 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
343 REFERENCES IN FILE CAPLUS (1907 TO DATE)

2/17/05

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FULL ESTIMATED COST                                     9.14       9.35

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FILE COVERS 1907 - 17 Feb 2005  VOL 142 ISS 8
FILE LAST UPDATED: 16 Feb 2005  (20050216/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l1/p
L2          14 L1/P

=> d abs fbib hitstr 1-14
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L2 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to polymorphs of zoledronic acid and zoledronate sodium salts, amorphous zoledronate sodium salts, processes for making the polymorphs and amorphous zoledronate sodium salt and pharmaceutical compns. containing the polymorphs and amorphous zoledronate sodium salt. For example, zoledronic acid crystal Form I was prepared by a phosphorylation reaction of 1-imidazoleacetic acid in the presence of phosphorous acid and phosphorus oxychloride in silicon oil as a diluent.

AN 2005:58222 CAPLUS

TI Processes for preparation of crystal forms of zoledronic acid and zoledronate sodium salts

IN Aronhime, Judith; Lifshitz-Liron, Revital

PA Teva Pharmaceutical Industries, Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005005447	A2	20050120	WO 2004-US21626	20040706

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

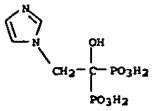
US 2003-484876P P 20030703

IT 118072-93-8P, Zoledronic acid
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of cryatal forms of zoledronic acid and amorphous and crystal forms of zoledronate sodium salts for dosage forms)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

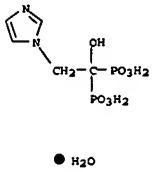
L2 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 165800-06-6P
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of crystal forms of zoledronic acid and amorphous and crystal forms of zoledronate sodium salts for dosage forms)

RN 165800-06-6 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis-, monohydrate (9CI) (CA INDEX NAME)



● H_2O

L2 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to processes for preparing and purifying zoledronic acid. Zoledronic acid was suspended in water at room temperature The pH of the suspension was adjusted to 14 by adding sodium hydroxide to obtain a clear solution Then the pH of the solution was adjusted to 1 by adding 32% HCl. The solution was cooled to 50° and was stirred at this temperature for 2.5 h. A massive precipitate of zoledronic acid was observed at 20°. The product was then isolated by filtration, washed with water and dried in a vacuum oven at 50° for 1.5 h and then in a vented oven at 65° for 24 h to obtain recrystd. zoledronic acid.

AN 2004:740139 CAPLUS

DN 141:243686

TI Process for purification of zoledronic acid

IN Lifshitz-Liron, Revital; Lidor-Hadas, Ramy

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SO PCT Int. Appl., 7 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004075860	A2	20040910	WO 2004-US5865	20040227

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003-449837P P 20030227

US 2004230076 A1 20041118 US 2004-789821 20040227

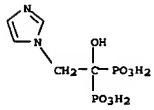
US 2003-449837P P 20030227

IT 118072-93-8P, Zoledronic acid
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(process for purification of zoledronic acid via reaction with sodium hydroxide and acidification with hydrochloric acid)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

L2 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L2 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB The effects of a series of 102 bisphosphonates on the inhibition of growth of Entamoeba histolytica and Plasmodium falciparum in vitro have been determined, and selected compds. were further investigated for their in vivo activity. Forty-seven compds. tested were active (IC50 < 200 μM) vs. E. Histolytica growth in vitro. The most active compds. (IC50 .apprx. 4-9 μM) were nitrogen-containing bisphosphonates with relatively large aromatic side chains. Simple n-alkyl-1-hydroxy-1,1-bisphosphonates, known inhibitors of the enzyme farnesylpyrophosphate (FPP) synthase, were also active, with optimal activity being found with C9-C10 side chains. However, numerous other nitrogen-containing bisphosphonates known to be potent FPP synthase inhibitors, such as risedronate or pamidronate, had little or no activity. Several pyridine-derived bisphosphonates were quite active (IC50 .apprx. 10-20 μM), and this activity was shown to correlate with the basicity of the aromatic group, with activity decreasing with increasing pKa values. The activities of all compds. were tested vs. a human nasopharyngeal carcinoma (KB) cell line to enable an estimate of the therapeutic index (TI). Five bisphosphonates were selected and then screened for their ability to delay the development of amebic liver abscess formation in an E. Histolytica infected hamster model. Two compds. were found to decrease liver abscess formation at 10 mg/kg i.p. with little or no effect on normal liver mass. With P. Falciparum, 35 compds. had IC50 values <200 μM in an in vitro assay. The most active compds. were also simple n-alkyl-1-hydroxy-1,1-bisphosphonates, having IC50 values around 1 μM. Five compds. were again selected for in vivo investigation in a Plasmodium berghei ANKA BALB/c mouse suppressive test. The most active compound, a C9 n-alkyl side chain containing bisphosphonate, caused an 80% reduction in parasitemia with no overt toxicity. Taken together, these results show that bisphosphonates appear to be useful lead compds. for the development of novel antiamebic and antimalarial drugs.

AN 2003:961354 CAPLUS

DN 140:138740

TI Effects of Bisphosphonates on the Growth of Entamoeba histolytica and Plasmodium Species in Vitro and in Vivo

AU Ghosh, Subhash; Chan, Julian M. W.; Lea, Christopher R.; Meints, Gary A.; Lewis, Jared C.; Tovian, Zev S.; Flessner, Ryan M.; Loftus, Timothy C.; Bruchhaus, Iris; Kendrick, Howard; Croft, Simon L.; Kemp, Robert G.; Kobayashi, Seiki; Nozaki, Tomoyoshi; Oldfield, Eric

CS Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL, 61801, USA

SO Journal of Medicinal Chemistry (2004), 47(1), 175-187
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

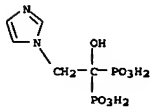
DT Journal

LA English

IT **118072-93-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and structure-activity relationship studies of bisphosphonates on growth of Entamoeba histolytica and Plasmodium species in vitro and in vivo)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB Provided is a novel method of making bisphosphonic acids, e.g. risedronic acid, including the step of combining a carboxylic acid, phosphorous acid, and a halophosphorous compound in the presence of a diluent that is an aromatic hydrocarbon or a silicone fluid. When the diluent is an aromatic hydrocarbon, a inert support or ortho-phosphoric acid codiluent is advantageously included. Thus, reaction of 3-pyridineacetic acid hydrochloride with phosphorus acid in PhMe containing silicone fluid followed by treatment with phosphorus oxychloride and workup gave risedronic acid monohydrate.

AN 2003:931375 CAPLUS

DN 139:381614

TI Use of certain diluents for making bisphosphonic acids

IN Lidor-Hadas, Rami; Harel, Zvi; Lifshitz-Liron, Revital; Kovalevski-Liron, Eti

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.

SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003097655	A1	20031127	WO 2003-US15676	20030519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2002-381284P	P 20020517
			US 2002-401313P	P 20020806
			US 2002-423337P	P 20021101
			US 2002-431838P	P 20021209
			US 2003-450193P	P 20030225
US 2004043967	A1	20040304	US 2003-442001	20030519
			US 2002-381284P	P 20020517
			US 2002-401313P	P 20020806
			US 2002-423337P	P 20021101
			US 2002-431838P	P 20021209
			US 2003-450193P	P 20030225
EP 1476451	A1	20041117	EP 2003-729005	20030519
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			US 2002-381284P	P 20020517
			US 2002-401313P	P 20020806
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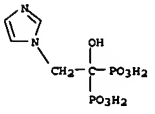
			US 2002-431838P	P 20021209
			US 2003-450193P	P 20030225
			WO 2003-US15676	W 20030519

OS CASREACT 139:381614

IT **118072-93-8P**, Zoledronic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(use of arom. hydrocarbon diluents in phosphorylation of carboxylic acid for prepn. of bisphosphonic acids)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB A process for preparing bisphosphonic acids, (M1O)(M2O)P(O)C(R1)(OH)P(O)(OM3) (OM4) (M1-M4 = H, monovalent cation; R1 = Me, 2-(1-imidazyl)methyl, 3-pyridylmethyl, 2-imidazo[1,2-a]pyridinylmethyl, H2N(CH2)n, n = 2-5, Me2NCH2CH2, n-PrN(Me)(CH2)5, etc.), characterized in that the reaction of synthesis is conducted in a reaction consisting of bisphosphonic acids, is described. Thus, reaction of γ-aminobutyric acid with PCl3 in the presence of tributylammonium chloride (preparation given), aqueous NaOH, and usual workup gave 31% sodium alendronate.

AN 2003:892788 CAPLUS

DN 139:365070

TI Preparation of biphosphonic acids and salts thereof

IN De Ferra, Lorenzo; Turchetta, Stefano; Massardo, Pietro; Casellato, Paolo

PA Chemi S.p.A., Italy

SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003093282	A1	20031113	WO 2002-IB4941	20021125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			IT 2002-MI908	A 20020429
EP 1504012	A1	20050209	EP 2002-807339	20021125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
			IT 2002-MI908	A 20020429
			WO 2002-IB4941	W 20021125

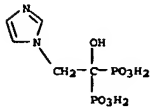
OS CASREACT 139:365070; MARPAT 139:365070

IT 118072-93-8P, Zoledronic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of biphosphonic acids and their pharmacol. active salts)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

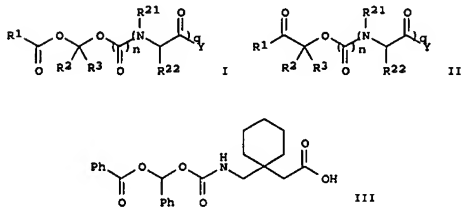
L2 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB The present invention provides a method for synthesizing 1-(acyloxy)alkyl derivs. I from 1-acylalkyl derivs. II [wherein n = 0-1; q = 0-1; provided that n and q = 0 unless Y = NRR' or OR; Y = NRR', OR, COR, PO(OR')R, or PO(OR')(OR); NRR', OR, COR, PO(OR')R, or PO(OR')(OR) = groups derived from drugs containing the indicated functional groups, with provisos; R1 = H or (un)substituted alkyl, (hetero)cycloalkyl, (hetero)arylalkyl, or a C23 bile acid moiety; R2 and R3 = independently H or (un)substituted (cyclo)alkyl, (cyclo)alkoxycarbonyl, aryl(alkyl), carbamoyl, or heteroaryl(alkyl); or R1 and either R2 or R3 may join together with the atoms to which they are attached to form an (un)substituted (hetero)cycloalkyl ring optionally fused to a (hetero)aryl or (hetero)cycloalkyl ring; or CR2R3 = (un)substituted (hetero)cycloalkyl; R21 = independently H or (un)substituted alkyl; R22 = independently H or (un)substituted (cyclo)alkyl, alkoxy(carbonyl), acyl, alkylamino, alkylthio, carbamoyl, aryl(alkyl), heteroaryl(alkyl), etc.; or pharmaceutically acceptable slats, hydrates, or solvates thereof]. The method typically proceeds stereospecifically, in high yield, does not require the use of activated intermediates and/or toxic compds., and is readily amenable to scale-up. The invention also provides 1-acylalkyl derivs. of known drug compds. and methods for synthesizing these 1-acylalkyl derivs. I and compns. thereof are useful as prodrugs (no data). For example, coupling of benzoin with p-nitrophenyl chloroformate using DMAP in CH2Cl2, followed by the addition of gabapentin in the presence of TEA and TMSCl CH2Cl2 gave 1-[[(α-benzoylbenzyloxy)carbonyl]aminom ethyl]-1-cyclohexaneacetic acid (90% over two steps). Oxidation with mCPBA in CH2Cl2 provided the α-(benzoyloxy)benzyl carbamate III (47%).

AN 2003:717749 CAPLUS

DN 139:245676

TI Methods for synthesis of 1-(acyloxy)alkyl carbamates and analogs as prodrugs from 1-acylalkyl derivatives and compositions thereof

IN Gallop, Mark A.; Xiang, Jia-Ning; Yao, Fenmei; Bhat, Laxminarayan; Zhou, Cindy X.

L2 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PA USA

SO U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

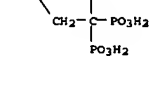
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003171303	A1	20030911	US 2002-167797	20020611
			US 2002-358603P	P 20020219
			US 2002-371535P	P 20020409
WO 2003077902	A1	20030925	WO 2002-US18691	20020611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2002-358603P	P 20020219
			US 2002-371535P	P 20020409
EP 1485082	A1	20041215	EP 2002-746514	20020611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			US 2002-358603P	P 20020219
			US 2002-371535P	P 20020409
			WO 2002-US18691	W 20020611

OS CASREACT 139:245676; MARPAT 139:245676

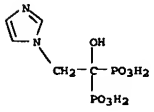
IT 118072-93-8DP, Zoledronate, prodrug derivative
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkoxyalkyl carbamates and analogs as prodrugs by oxidation of acylalkyl derivs.)

RN 118072-93-8 CAPLUS

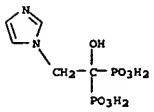
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



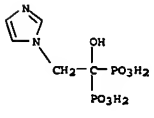
L2 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AB Stirring imidazole with Et bromoacetate in MeCN in the preaence of KF/AlCl3 at 30° for 3 h gave 77.5% 1H-imidazole-1-acetic acid Et ester, which waa refluxed with water for 7 h to give 1H-imidazole-1-acetic acid (I). Treating I with PCl3 and 85% H3PO4 in the presence of PEG-400 at 75° for 4 h gave 50.7% zoledronic acid.
AN 2003:159671 CAPLUS
DN 139:381537
TI Synthesis of zoledronic acid
AU Zhu, Ju; Zhou, You-jun; Lu, Jia-guo; Liu, Jian-fei; Zhang, Wan-nian
CS Dept. of Medicinal Chemistry, College of Pharmacy, Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SO Zhongguo Xinyao Zazhi (2003), 12(1), 39-40
CODEN: ZXZHA6; ISSN: 1003-3734
PB Zhongguo Xinyao Zazhishe
DT Journal
LA Chinese
OS CASREACT 139:381537
IT 118072-93-8P, Zoledronic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(syntheais of zoledronic acid)
RN 118072-93-8 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L2 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AB Title compound, a new drug for treating hypercalcemia, was synthesized via substitution imidazole with Et bromoacetate, after hydrolyzation to afford imidazol-1-ylacetic acid, then reacted with phosphoric acid with the presence of phosphorua trichloride, giving the product with overall yield 27.0%. By using TEBA instead of BBDE chloride as phase transfer catalyst, and imidazole acetic acid instead of its HCl salt as the key intermediate, this process can easily obtain the product in good quality and yield.
AN 2003:30096 CAPLUS
DN 139:69193
TI Improved process for the synthesis of zoledronic acid as a new drug for treating hypercalcemia
AU Li, Jiaming; Tong, Yuanfeng; Zhang, Yong
CS Department of Pharmaceutical Chemistry, Anhui College of Traditional Chinese Medicine, Hefei, 230038, Peop. Rep. China
SO Zhongguo Yaowu Huaxue Zazhi (2002), 12(3), 164-165, 186
CODEN: ZYHZEF; ISSN: 1005-0108
PB Zhongguo Yaowu Huaxue Zazhi Bianjibu
DT Journal
LA Chinese
OS CASREACT 139:69193
IT 118072-93-8P, Zoledronic acid
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved process for the synthesis of zoledronic acid)
RN 118072-93-8 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



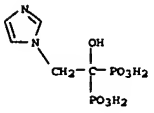
L2 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AB A review covering the 24 new drugs approved by the Food and Drug Administration in the year 2001. Therapeutics are grouped according to the following coded areas: (A) agents affecting neurotransmitters and cytokines, (B) antiinflammatory agents, (C) hormone related agents, (D) anti-infectious agents, and (E) miscellaneous agents. A synopsis for each drug includes a brief description of its medical utility, a mechanism of action if known, a chemical structure, and a pathway for its synthesis.
AN 2002:720795 CAPLUS
DN 138:280580
TI FDA new drug approvals in 2001
AU Zhao, Kang; He, Lan; Reiner, John
CS The College of Pharmaceuticals and Biotechnology, Tianjin University, Peop. Rep. China
SO Frontiers of Biotechnology & Pharmaceuticals (2002), 3, 400-413
CODEN: FBPRBL
PB Science Press New York Ltd.
DT Journal; General Review
LA English
IT 118072-93-8P, Zoledronic acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FDA new drug approvals in 2001)
RN 118072-93-8 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AB Bisphosphonates (BPs) are pyrophosphate analogs in which the oxygen in P-O-P has been replaced by a carbon, resulting in a metabolically stable P-C-P structure. Pamidronate (1b, Novartis), a second-generation BP, was the starting point for extensive SAR studies. Small changes of the structure of pamidronate lead to marked improvements of the inhibition of osteoclastic resorption potency. Alendronate (1c, MSD), with an extra methylene group in the N-alkyl chain, and olpadronate (1h, Gador), the N,N-di-Me analog, are about 10 times more potent than pamidronate. Extending one of the N-Me groups of olpadronate to a pentyl substituent leads to ibandronate (1k, Roche, Boehringer-Mannheim), which is the most potent close analog of pamidronate. Even slightly better antiresorptive potency is achieved with derivs. having a Ph group linked via a short aliphatic tether of three to four atoms to nitrogen, the second substituent being preferentially a Me group (e.g., 4g, 4j, 5d, or 5r). The most potent BPs are found in the series containing a heteroarom. moiety (with at least one nitrogen atom), which is linked via a single methylene group to the geminal bisphosphonate unit. Zoledronic acid (6i), the most potent derivative, has an ED50 of 0.07 mg/kg in the TPTX in vivo assay after s.c. administration. It not only shows by far the highest therapeutic ratio when comparing resorption inhibition with undesired inhibition of bone mineralization but also exhibits superior renal tolerability. Zoledronic acid (6i) has thua been selected for clin. development under the registered trade name Zometa. The results of the clin. trials indicate that low doses are both efficacious and safe for the treatment of tumor-induced hypercalcemia, Paget's disease of bone, osteolytic metastases, and postmenopausal osteoporosis.
AN 2002:539062 CAPLUS
DN 137:226194
TI Highly Potent Geminal Bisphosphonates. From Pamidronate Disodium (Aredia) to Zoledronic Acid (Zometa)
AU Widler, Leo; Jaeggi, Knut A.; Glatt, Markus; Mueller, Klaus; Bachmann, Rolf; Bisping, Michael; Born, Anne-Ruth; Cortesi, Reto; Guiglia, Gabriela; Jeker, Heidi; Klein, Remy; Ramseier, Ueli; Schmid, Johann; Schreiber, Gerard; Seltenmeyer, Yves; Green, Jonathan R.
CS Arthritis and Bone Metabolism Therapeutic Area, Novartis Pharma Research, Basel, CH-4002, Switz.
SO Journal of Medicinal Chemistry (2002), 45(17), 3721-3738
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:226194
IT 118072-93-8P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(biaphosphonates preparation and structure-related bone antiresorptive properties)
RN 118072-93-8 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

L2 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RE.CNT 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB Two new series of fused aza-heteroarylbisphosphonates which are structurally quite different from incadronate (YM175), and related compds. were synthesized and evaluated for antiresorptive activity using a parathyroid hormone(PTH)-induced hypercalcemia model in rats (PIH model). Among these compds., several exhibited more potent antiresorptive activity than pamidronate. In particular, [1-hydroxy-2-(imidazo[1,2-a]pyridin-3-yl)ethylidene]bisphosphonic acid (5b, minodronate) was 100-fold more potent than pamidronate in not only the PIH model, but also in an immobilization bone atrophy model in rats (DA model), and was selected for clin. development. The structure-activity relations in these new series of bisphosphonates are discussed. X-ray crystal structures of [1-hydroxy-2-(imadazo[1,2-a]pyridin-2-yl)ethylidene]bisphosphonic acid (5a) (space group P21/c, Rw = 0.063, Z = 4) and 5b (space group P.hivin.1, Rw = 0.099, Z = 2) were determined

AN 1998:758024 CAPLUS

DN 130:110331

TI Studies on novel bone resorption inhibitors. II. Synthesis and pharmacological activities of fused aza-heteroarylbisphosphonate derivatives

AU Takeuchi, Makoto; Sakamoto, Shuichi; Kawamuki, Kousei; Kurihara, Hiroyuki; Nakahara, Hideaki; Isomura, Yasuo

CS Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., Tsukuba, 305-8585, Japan

SO Chemical & Pharmaceutical Bulletin (1998), 46(11), 1703-1709
CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

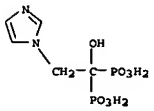
LA English

OS CASREACT 130:110331

IT **118072-93-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(antiresorptive activity)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L2 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB The azabisphosphonic acids R6R7NCR4R5(CR2R3)nCR1(PO3H2)2 [n = 0, 1-6; R1 = H, OH, alkyl, alkoxy, halo, etc.; R2-5 H, (un)substituted hydrocarbyl, etc.; R6, R7 = R2, (un)substituted pyridyl or (un)substituted amino; R6R7N, R4R6CN or R2R6CN = (un)substituted N-containing heterocyclyl; R2R4C and R4R5C = (un)substituted carbocyclyl] and their salts or hydrolyzable esters are prepared as postemergence herbicides.

AN 1998:186482 CAPLUS

DN 128:240717

TI Preparation of herbicidal azabisphosphonic acids

IN Fisher, Karl J.; Woolard, Frank X.; Leadbetter, Michael R.; Gerdes, John M.

PA Zeneca Ltd., UK

SO U.S., 43 pp., Cont.-in-part of U.S. Ser. No. 133,722, abandoned.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5728650	A	19980317	US 1995-418970	19950407
				US 1993-133722 B2	19931007
	TW 401276	B	20000811	TW 1994-83109255	19941005
				US 1993-133722 A	19931007
	ZA 9407814	A	19950814	ZA 1994-7814	19941006
				US 1993-133722 A	19931007
	IL 111180	A1	19990922	IL 1994-111180	19941006
				US 1993-133722 A	19931007
	CA 2173607	AA	19950420	CA 1994-2173607	19941007
				US 1993-133722 A	19931007
	CN 1134657	A	19961030	CN 1994-194096	19941007
				US 1993-133722 A	19931007
	HU 74893	A2	19970228	HU 1996-839	19941007
				US 1993-133722 A	19931007
	CA 2217655	AA	19961010	CA 1996-2217655	19960408
				US 1995-418970 A	19950407
	WO 9631124	A1	19961010	WO 1996-US4869	19960408
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
				US 1995-418970 A	19950407
	AU 9654475	A1	19961023	AU 1996-54475	19960408
				US 1995-418970 A	19950407
				WO 1996-US4869 W	19960408
	EP 820230	A1	19980128	EP 1996-911660	19960408
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
				US 1995-418970 A	19950407
				WO 1996-US4869 W	19960408
	CN 1181690	A	19980513	CN 1996-193132	19960408
				US 1995-418970 A	19950407
	BR 9604975	A	19980609	BR 1996-4975	19960408
				US 1995-418970 A	19950407
				WO 1996-US4869 W	19960408
	JP 11503429	T2	19990326	JP 1996-530540	19960408

L2 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408
	NO 9704619	A	19971006	NO 1997-4619		19971006
				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408

PATENT FAMILY INFORMATION:

FAN 1995:750617

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9510188	A2	19950420	WO 1994-GB2183	19941007
	WO 9510188	A3	19950504		
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	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1993-133722	A 19931007
	TW 401276	B	20000811	TW 1994-83109255	19941005
				US 1993-133722	A 19931007
	ZA 9407814	A	19950814	ZA 1994-7814	19941006
				US 1993-133722	A 19931007
	IL 111180	A1	19990922	IL 1994-111180	19941006
				US 1993-133722	A 19931007
	CA 2173607	AA	19950420	CA 1994-2173607	19941007
				US 1993-133722	A 19931007
	AU 9477901	A1	19950504	AU 1994-77901	19941007
	AU 690581	B2	19980430		
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007
	EP 722268	A1	19960724	EP 1994-928482	19941007
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007
	CN 1134657	A	19961030	CN 1994-194096	19941007
				US 1993-133722	A 19931007
	HU 74893	A2	19970228	HU 1996-839	19941007
				US 1993-133722	A 19931007
	BR 9407762	A	19970304	BR 1994-7762	19941007
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007
	JP 09506075	T2	19970617	JP 1994-511442	19941007
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007
	NO 9601389	A	19960603	NO 1996-1389	19960403
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007
	FI 9601520	A	19960527	FI 1996-1520	19960404
				US 1993-133722	A 19931007
				WO 1994-GB2183	W 19941007

FAN 1996:705780

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631124	A1	19961010	WO 1996-US4869	19960408

L2 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

	W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
				US 1995-418970	A	19950407
	US 5728650	A	19980317	US 1995-418970		19950407
				US 1993-133722	B2	19931007
	AU 9654475	A1	19961023	AU 1996-54475		19960408
				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408
	EP 820230	A1	19980128	EP 1996-911660		19960408
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				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408
	BR 9604975	A	19980609	BR 1996-4975		19960408
				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408
	JP 11503429	T2	19990326	JP 1996-530540		19960408
				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408
	NO 9704619	A	19971006	NO 1997-4619		19971006
				US 1995-418970	A	19950407
				WO 1996-US4869	W	19960408

OS MARPAT 128:240717

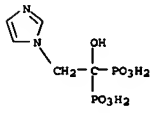
IT **118072-93-8P**

RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation as herbicide)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB Moderate to poor yields of 1-hydroxy-1,1-bisphosphonates, prepared by reacting a carboxylic acid with PCl3 and H3PO3, can be substantially increased by running the reaction in methanesulfonic acid. The target compds. thus prepared are (3-amino-1-hydroxypropylidene)bis[Phosphonic acid], (4-amino-1-hydroxybutylidene)bis[Phosphonic acid], etc., and alendronate sodium.

AN 1995:947515 CAPLUS

DN 124:117423

TI Preparation of (4-Amino-1-Hydroxybutylidene)bisphosphonic Acid Sodium Salt, MK-217 (Alendronate Sodium). An Improved Procedure for the Preparation of 1-Hydroxy-1,1-bisphosphonic Acids

AU Kieczykowski, Gerard R.; Jobson, Ronald B.; Melillo, David G.; Reinhold, Donald. F.; Grenda, Victor J.; Shinkai, Ichiro

CS Merck Research Laboratories, Merck and Co. Inc., Rahway, NJ, 07065, USA

SO Journal of Organic Chemistry (1995), 60(25), 8310-12
CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

OS CASREACT 124:117423

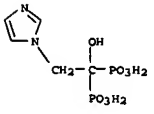
IT **118072-93-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of (aminohydroxybutylidene)bisphosphonates)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L2 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AB R1CH2CR2(PO3H2)2 (I; R1 = 5-membered heteroaryl comprising 2-4 N atoms or 1-2 N atoms plus an O or S atom with optional substituents; R2 = H, OH, NH2, alkylthio, halo) and their salts, useful as pharmaceuticals, are prepared PCl3 was added to a mixture of 0.053 mol imidazol-4-ylacetic acid HCl in 85% H3PO4 and PhCl at 100° to give 40% title acid I (R1 = imidazol-4-ly, R2 = OH) (II). A tablet formulation was prepared from II.2Na 100.0, lactose 100.0, corn starch 47.0, and Mg stearate 3.0 g.

AN 1989:24084 CAPLUS

DN 110:24084

TI Preparation of alkylenediphosphonic acids and salts, and pharmaceutical compositions containing them

PA Ciba-Geigy A.-G., Switz.

SO Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 2

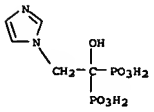
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63150291	A2	19880622	JP 1987-292198	19871120
	JP 2744238	B2	19980428		
				CH 1986-4666	A 19861121
	EP 275821	A1	19880727	EP 1987-810664	19871116
	EP 275821	B1	19920226		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
				CH 1986-4666	A 19861121
	AT 72816	E	19920315	AT 1987-810664	19871116
				CH 1986-4666	A 19861121
				EP 1987-810664	A 19871116
	ES 2038692	T3	19930801	ES 1987-810664	19871116
				CH 1986-4666	A 19861121
	IL 84497	A1	19941021	IL 1987-84497	19871116
				CH 1986-4666	A 19861121
	FI 8705096	A	19880522	FI 1987-5096	19871118
	FI 87570	B	19921015		
	FI 87570	C	19930125		
				CH 1986-4666	A 19861121
	CA 1338937	A1	19970225	CA 1987-552209	19871119
				CH 1986-4666	A 19861121
	DK 8706095	A	19880522	DK 1987-6095	19871120
	DK 174098	B1	20020617		
				CH 1986-4666	A 19861121
	NO 8704856	A	19880524	NO 1987-4856	19871120
	NO 173446	B	19930906		
	NO 173446	C	19931215		
				CH 1986-4666	A 19861121
	AU 8781453	A1	19880526	AU 1987-81453	19871120
	AU 607722	B2	19910314		
				CH 1986-4666	A 19861121
	ZA 8708698	A	19880727	ZA 1987-8698	19871120
				CH 1986-4666	A 19861121
	HU 46330	A2	19881028	HU 1987-5160	19871120
	HU 199150	B	19900129		
				CH 1986-4666	A 19861121
	DD 270533	A5	19890802	DD 1987-309267	19871120
				CH 1986-4666	A 19861121

PATENT FAMILY INFORMATION:

L2 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
FAN 1991:62355

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4939130	A	19900703	US 1989-315962	19890227
				CH 1986-4666 A	19861121
				US 1987-120284 B2	19871113
	AT 72816	E	19920315	AT 1987-810664	19871116
				CH 1986-4666 A	19861121
				EP 1987-810664 A	19871116

OS MARPAT 110:24084
IT 118072-93-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as calcium metabolism regulator)
RN 118072-93-8 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI)
(CA
INDEX NAME)



2/17/05

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            945 PURIFICATIONS
         305453 PURIFICATION
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         274930 PURIFN
            236 PURIFNS
         275033 PURIFN
                  (PURIFN OR PURIFNS)
         449844 PURIFICATION
                  (PURIFICATION OR PURIFN)
        1217033 PH
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        1221098 PH
                  (PH OR PHS)
L3        65924 PURIFICATION AND PH

=> s purifying by changing pH
          31268 PURIFYING
         120733 CHANGING
             19 CHANGINGS
         120749 CHANGING
                  (CHANGING OR CHANGINGS)
        1217033 PH
           9244 PHS
        1221098 PH
                  (PH OR PHS)
L4            0 PURIFYING BY CHANGING PH
                  (PURIFYING(1W)CHANGING(W)PH)

=> s purif? by changing pH
         759574 PURIF?
         120733 CHANGING
             19 CHANGINGS
         120749 CHANGING
                  (CHANGING OR CHANGINGS)
        1217033 PH
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                  (PH OR PHS)
L5            1 PURIF? BY CHANGING PH
                  (PURIF?(1W)CHANGING(W)PH)

=> d abs fbib hitstr
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2/17/05

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AB The apparatus includes a section for introducing the water to be treated, a
section having a plurality of filtering materials (e.g., barite, limestone) for **purification** and **changing pH**, and
a section for discharging the treated water.
AN 1996:664500 CAPLUS
DN 125:283963
TI Apparatus for purification of wastewater and water in natural area by filtration
IN Tsuzuki, Koichi; Mizumori, Takashi; Takagi, Takeo; Yoda, Hiroaki; Okajima,
Hiroaki
PA Hitachi Ltd, Japan; Hitachi Tsuchiura Eng
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08206674	A2	19960813	JP 1995-14931	19950201
				JP 1995-14931	19950201

2/17/05

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          9244 PHS
       1221098 PH
                  (PH OR PHS)
L6           1 L2 AND PURIF? AND PH

=> d abs fbib hitstr
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L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to processes for preparing and purifying zoledronic acid. Zoledronic acid was suspended in water at room temperature
The pH of the suspension was adjusted to 14 by adding sodium hydroxide to obtain a clear solution Then the pH of the solution was adjusted to 1 by adding 32% HCl. The solution was cooled to 50° and was stirred at this temperature for 2.5 h. A massive precipitate of zoledronic acid
was observed at 20°. The product was then isolated by filtration, washed with water and dried in a vacuum oven at 50° for 1.5 h and then in a vented oven at 65° for 24 h to obtain recrystd. zoledronic acid.

AN 2004:740139 CAPLUS

DN 141:243686

TI Process for purification of zoledronic acid

IN Lifshitz-Liron, Revital; Lidor-Hadas, Ramy

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SO PCT Int. Appl., 7 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

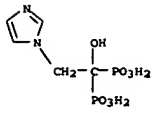
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004075860	A2	20040910	WO 2004-US5865	20040227
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2003-449837P	P 20030227
	US 2004230076	A1	20041118	US 2004-789821	20040227
				US 2003-449837P	P 20030227

IT 118072-93-8P, Zoledronic acid
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(process for purification of zoledronic acid via reaction with sodium hydroxide and acidification with hydrochloric acid)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



2/17/05

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           945 PURIFICATIONS
        305453 PURIFICATION
                 (PURIFICATION OR PURIFICATIONS)
        274930 PURIFN
           236 PURIFNS
        275033 PURIFN
                 (PURIFN OR PURIFNS)
        449844 PURIFICATION
                 (PURIFICATION OR PURIFN)
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L8           1 L7 AND PURIFICATION BY CHANGING PH

=> d abs
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